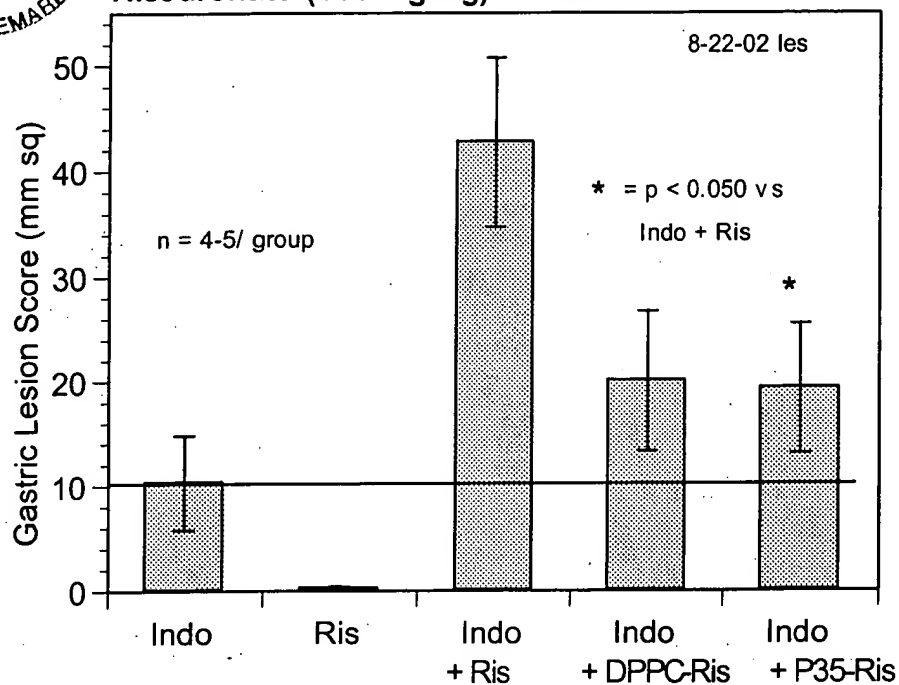


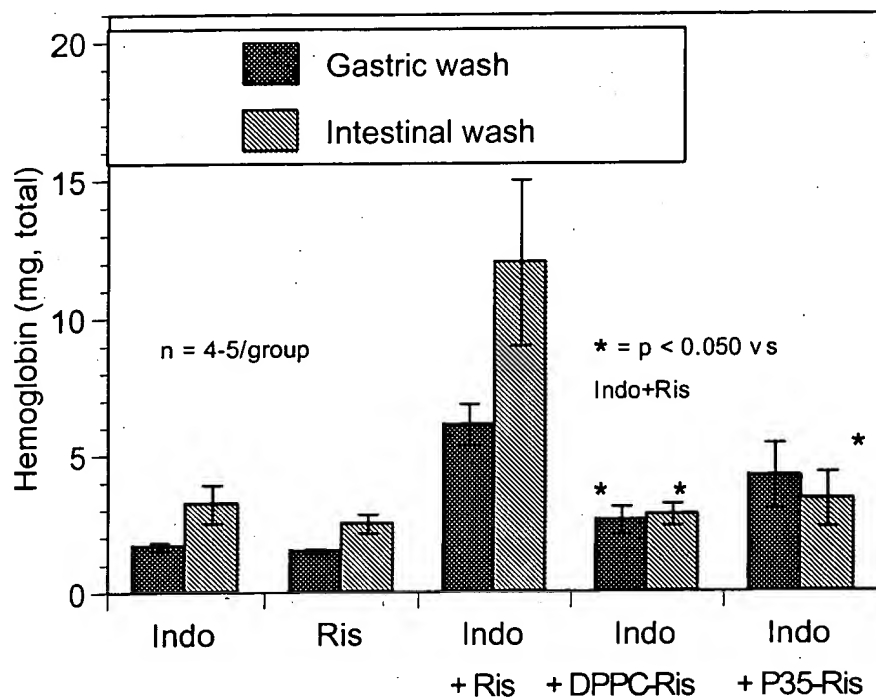


**Protective Effect of DPPC and P35 Against  
Challenge of Indomethacin (Indo, 40 mg/kg) and  
Risedronate (100 mg/kg) in Rats**



**Protective Effect of DPPC and P35 Against  
Challenge of Indomethacin (Indo, 40 mg/kg) and  
Risedronate (100 mg/kg) in Rats**

8-22-02 hg





## Bioavailability of Risedronate (Ris)<sup>α</sup> and PC-Risedronate (PC-Ris)<sup>β</sup> in Rats

|       | 0.5 hour |        | 1 hour |        | 2 hour |        | 4 hour |        | 8 hour |        | 24 hour |        |
|-------|----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|---------|--------|
|       | Ris      | PC-Ris | Ris    | PC-Ris | Ris    | PC-Ris | Ris    | PC-Ris | Ris    | PC-Ris | Ris     | PC-Ris |
| 14863 | 23464    | 2678   | 14267  | 3062   | 1294   | 2733   | 2566   | 235    | 3287   | 73     | 85      |        |
| 5529  | 2459     | 2660   | 10914  | 13952  | 14689  | 1162   | 2162   | 823    | 555    | 85     | 74      |        |
| 4299  | 3354     | 17457  | 2632   | 1907   | 1599   | 777    | 1352   | 471    | 379    | 168    | 146     |        |
| 16616 | 2347     | 5174   | 2348   | 7349   | 5972   | 1741   | 15557  | 466    | 621    | 78     | 226     |        |
| 34649 | 8486     | 1714   | 3683   | 1057   | 6160   | 2326   | 7264   | 507    | 538    |        |         |        |
| 1304  | 2636     | 1416   | 11137  | 983    | 7340   | 5110   | 2811   | 384    | 5210   |        |         |        |
| 8011  | 1262     | 1283   | 2165   | 1347   | 1217   | 1639   | 2155   | 312    | 5987   |        |         |        |
| 8733  | -----    | 2085   | 860    | 1588   | 7168   | 2186   | 2453   | 366    | 1128   |        |         |        |
| 11751 | 6287     | 4398   | 6001   | 3906   | 5684   | 2209   | 4540   | 446    | 2213*  | 101    | 133     |        |
| ±3742 | ±2997    | ±1915  | ±1842  | ±1615  | ±1594  | ±471   | ±1698  | ±63    | ±813   | ±23    | ±35     |        |

<sup>α</sup> Ris, at a specific activity of 100  $\mu\text{Ci/mg}$  was administered to fasted male Sprague Dawley rats (250-300g) at a final dose of 1 mg/kg (or  $\sim 65 \times 10^6$  cpm/rat).

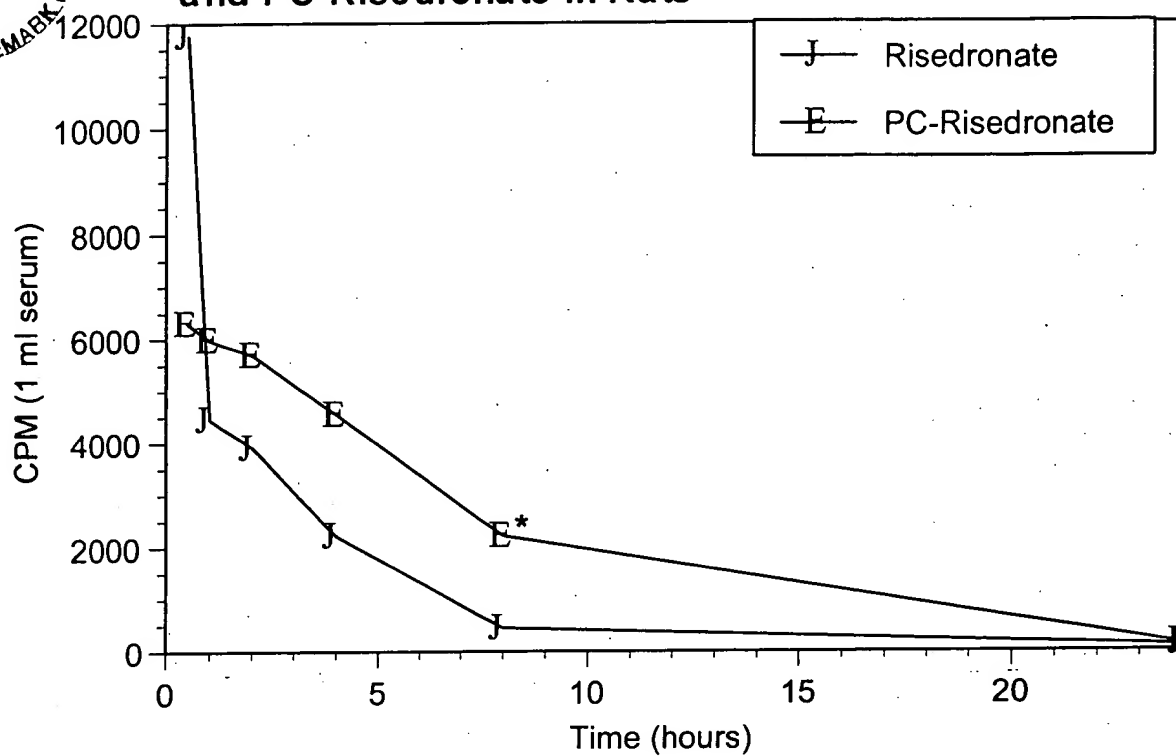
<sup>β</sup> Phospholipon 90 G [containing 93% phosphatidylcholine (PC)] was initially dissolved in chloroform. The solvent was removed by evaporation under nitrogen in tubes to which labeled Ris was added to come to a final PC-Ris formulation at a weight ratio of 1 part Phospholipon 90G: 1 part risedronate.

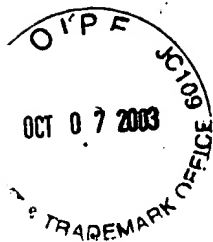
\* Indicates  $p < 0.05$  vs Ris



# Comparison of the Bioavailability of Risedronate and PC-Risedronate in Rats

8-15+8-22-02





## Bioavailability of C<sup>14</sup>- Risedronate Alone and in Association with PC in Rats Dosed Before and After Feeding

Dose/rat=11.89 x 10<sup>6</sup> ± 0.24

Risedronate-rats fed immediately after dosing (CPM/ml plasma)

| <u>Time</u><br>(hours) | 0.5        | 1          | 2           | 4          | 8          | 24         |
|------------------------|------------|------------|-------------|------------|------------|------------|
|                        | 441        | 229        | 861         | 457        | 87         | 152        |
|                        | 962        | 467        | 458         | 437        | 113        | 82         |
|                        | 18,436     | 532        | 894         | 377        | 197        | 43         |
|                        | 534        | 552        | 697         | 324        | 99         | 115        |
|                        | 159        | 4216       | 157         | 213        | -----      | 122        |
|                        | 837        | 1073       | 945         | 10648      | 188        | 40         |
|                        | 462        | 795        | 1135        | 4985       | 200        | 144        |
|                        | <u>970</u> | <u>273</u> | <u>1493</u> | <u>656</u> | <u>100</u> | <u>197</u> |
|                        | 2849.9     | 1016.8     | 830.2       | 2811.8     | 140.3      | 111.7      |
|                        | ±2228.9    | ±467.1     | ±144        | ±1325.6    | ±18.2      | ±19.3      |

Risedronate:PC-rats fed immediately after dosing (CPM/ml plasma)

| <u>Time</u><br>(hours) | 0.5          | 1          | 2           | 4          | 8         | 24        |
|------------------------|--------------|------------|-------------|------------|-----------|-----------|
|                        | 1291         | 6205       | 1492        | 410        | 134       | 303       |
|                        | 520          | 13350      | 11724       | 863        | 192       | 261       |
|                        | 4463         | 943        | 5561        | 1750       | 1959      | 99        |
|                        | 1321         | 10217      | 3689        | 806        | 354       | 163       |
|                        | 2132         | 283        | 2560        | 10746      | 188       | 115       |
|                        | 1447         | 393        | 510         | 539        | 119       | 141       |
|                        | 720          | 642        | 1152        | 636        | 143       | 64        |
|                        | <u>14007</u> | <u>419</u> | <u>5358</u> | <u>214</u> | <u>59</u> | <u>51</u> |
|                        | 3237.5       | 4056.3     | 4005.5      | 1995.5     | 393.2     | 149.5     |
|                        | ±1598.6      | ±1847.7    | ±1286.6     | ±1260.6    | ±225.7    | ±32       |



**Risedronate-rats fed 30 minutes before dosing (CPM/ml plasma)**

| <u>Time</u><br>(hours) | 0.5         | 1          | 2          | 4          | 8         | 24 |
|------------------------|-------------|------------|------------|------------|-----------|----|
| 1605                   | 201         | 575        | 155        | 334        | 35        |    |
| 316                    | 1315        | 446        | 141        | 164        | 19        |    |
| 486                    | 3618        | 753        | 129        | 181        | 19        |    |
| 1291                   | 793         | 517        | 162        | 116        | 14        |    |
| 334                    | 450         | 3285       | 410        | 5176       | 128       |    |
| 420                    | 404         | 558        | 185        | 211        | 48        |    |
| 413                    | 270         | 647        | 323        | 207        | 44        |    |
| <u>538</u>             | <u>1194</u> | <u>347</u> | <u>288</u> | <u>261</u> | <u>36</u> |    |
| 675.4                  | 1029.5      | 891        | 224.1      | 831.3      | 42.7      |    |
| ±173.1                 | ±159.1      | ±343.2     | ±36.5      | ±621.1     | ±4.3      |    |

**Risedronate:PC- rats fed 30 minutes before dosing (CPM/ml plasma)**

| <u>Time</u><br>(hours) | 0.5        | 1          | 2          | 4          | 8         | 24 |
|------------------------|------------|------------|------------|------------|-----------|----|
| 3479                   | 256        | 300        | 261        | 248        | 40        |    |
| 447                    | 180        | 444        | 639        | 201        | 56        |    |
| 9917                   | 1849       | 2004       | 400        | 146        | 59        |    |
| 2711                   | 273        | 336        | 377        | 229        | 63        |    |
| 315                    | 243        | 450        | 427        | 171        | 71        |    |
| 2823                   | 271        | 581        | 267        | 295        | 71        |    |
| 260                    | 3412       | 522        | 498        | 154        | 48        |    |
| <u>470</u>             | <u>218</u> | <u>456</u> | <u>349</u> | <u>214</u> | <u>43</u> |    |
| 2552.8                 | 837.8      | 636.7      | 402.3      | 207.3      | 56.4      |    |
| ±1151.3                | ± 418.3    | ±198       | ±43.9      | ±17.9      | ±4.3      |    |

# **Bioavailability of C<sup>14</sup> - Risedronate Alone and in Association with PC in Rats Dosed Before and After Feeding**

